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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/730,716	12/06/2000	Young Chul Sung	G&C 118.6-US-01	7984

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EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	11

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/730,716	SUNG ET AL.	
	Examin r	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 01/01/01 has been acknowledged.

Claims 1-22 are canceled.

Claims 23-30 are newly filed claims and are examined in this office action.

► ***Applicants are required to follow Amendment Practice under revised 37 CFR §1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm).***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Priority

The applicant argues that a certify copy of priority application and English translation were provided at the time of filing. The instant application contains the copy of Korean application No.55129. However, a certified English translation of the Korea application as required by 35 U.S.C. 119(b) was not found. To comply with 35 U.S.C. 119(b) requirements a certified copy of English translation has been requested.

Claim Rejections - 35 USC § 112, 1st Paragraph

Claims 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a vaccine comprising pTV-SIV/GE+pTV-SIV/pol that prevents SIV infection in rhesus monkeys, does not reasonably provide enablement for any other vaccines that prevents AIDS in rhesus monkey. The specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to arguments

The applicant fails to address the enablement rejection especially in view of state of the AIDS vaccine art and the guidance provided in the specification. Interpreting the results of figure-4 in the specification, the applicant argues that the DNA vaccine of the present invention show prevention of AIDS in rhesus monkey (response, page 9 para.2). The applicant concluded that one skill in the art would have a reasonable expectation of success in practicing the invention as claimed with variations that facilitate immunogenicity (response, page 9, para.3)

However, this is found NOT persuasive because applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). At best the specification only teaches that intra muscular injection of pTV-SIV/GE and pTV-SIV/pol into rhesus monkeys prevents SIVmac239 infection after immunization (spec. pages 22-25). The specification fails to provide any evidence that establishes that besides pTV-SIV/GE and pTV-SIV/pol any other structural and functional combination of plasmid constructs encoding i) SIV's gag, dpol, env and rev gene wherein in the plasmid lacks vpr, tat and nef genes and ii) SIV's pol gene encoding transcriptase and intergrase gene operably linked to any secretory protein would prevent SIV infection and/or AIDS in rhesus monkey.

The earlier office action clearly provided the evidence regarding the unpredictability in the art of AIDS vaccine. The difficulty in vaccine development in AIDS prevention and treatment has been well recognized due to non-cross reacting between different strains and lack of animal models. Daniel et al. (Science 258:1938-1941, 1992) states that the difficulty in AIDS vaccine development is the persistent, unrelenting nature of HIV and SIV infection once infection is initiated (Daniel, Abstract) and the large number of HIV-1 strains that are non-or minimally cross-neutralizing (Daniel, page 1938, first para). The difficulty in achieving protection against HIV and SIV has been borne out to varying degrees by vaccine trials in animal models including the limited success in chimpanzee trials (Daniel, page 1938, middle col. sec. parag. to the end). Furthermore, Smith et al. (Viral Immunol 13:343-351, 2000) state that it has

become increasingly clear that the use of classic vaccine approaches are not sufficient to develop a successful vaccine against human immunodeficiency virus (HIV) or its simian counterpart, simian immunodeficiency virus (SIV). Subunit vaccines comprising killed or inactivated virus, recombinant vaccinia virus expressing SIV proteins, and synthetic peptides representing immunogenic regions of the envelope protein are some of the vaccine candidates that have been tested in the SIV-rhesus macaque model system. These vaccines have demonstrated that complete protection from infection and progression to disease is extremely hard to achieve against SIV. An effective vaccine will likely elicit both a humoral and cellular immune response, but a clear understanding of the specific immunological correlates of protection in these studies still awaits further investigation (Smith, page 343).

In instant case the use of DNA based vaccines to prevents AIDS is not routine in the art and without sufficient guidance to a specific genetic construct and its efficacy to prevent AIDS the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claim Rejections - 35 USC § 103

Applicant's arguments with respect to claims 23-25 have been considered but are moot in view of the new ground(s) of rejection below:

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al (Viral Immunol 13:343-51, 2000, *ref of record*) in view of Daniel et al. (Science 258:1938-1941, 1992, *ref of record*).

The invention as claimed is drawn to a plasmid vector carrying SIV gag, dpol, env and rev genes, wherein the plasmid lacks vpr, tat and nef genes.

Smith teaches a DNA based SIV vaccine composition. The cited art teaches SIVsmH3/B7 expression construct comprising SIV gag, pol, env and rev genes (page 346, fig-1). The cited art further teaches a vector that comprises a deletion of SIV vpx/vpr and tat genes (fig-1 B). However the cited art does not teach a SIV plasmid construct that comprises a deletion in nef gene.

Daniel teaches a live attenuated SIV vaccine with a deletion in the nef gene (abstract, page 1939, table2 and 3). The cited art further teaches that use of deletion mutants eliminates the possibility of reversion and helps to ensure the safety of inoculation with attenuated virus vaccine (page 1941, col.1 para.2).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the SIV plasmid construct as taught by Smith, by deleting nef region as taught by Daniel. One would have been motivated to do so to eliminate the possibility of reversion and helps to ensure the safety of inoculation with attenuated virus vaccine. One would have a reasonable expectation of success, since making a mutation or deletion in SIV genome has been routine in the art. Thus, the claimed invention is *prima facie* obvious in view of cited prior art of record.

Claims 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gŏttlinger et al (US 6479281, 2002) in view of Morris-Vasios et al. (J Virol 62:349-353, 1988).

The instant claims are directed to a plasmid carrying a SIV-derived pol gene encoding for a reverse transcriptase and an integrase, wherein the 5'-end of pol gene is fused to signal sequence of a secretion protein.

Gŏttlinger teaches a lentiviral vector system, wherein the vector system further comprising a pol vector encoding lentiviral pol-proteins operably linked to promoter and a polyadenylaltion sequence (col.27 lines 28-31). The cited art further teaches that the lentiviral pol protein that is selected form simian immunodeficiency virus (SIV). However, Gŏttlinger does not teach the fusion of SIV pol gene to a signal sequence of a secretion protein.

Morris-Vasios teaches the fusion of the 5'-end the gene encoding avian sarcoma-leukosis retrovirus pol-endo protein to a secretory signal sequences obtained from interleukin-2 receptor gene (Abstract, page 351, left col. line 2-3, page 352, fig-5). The cited art further teaches the c-

terminal portion of the pol gene product is required for the integration of proviral DNA into a host cell chromosome (page 349, col.1). The cited art further teaches a recombinant p36 pol-endo protein containing a N-terminal secretory signal (page 352, fig-1). The cited art further teaches that addition of the secretory signal sequence directs the protein to secretory pathway (page 352, col.1). The cited art further teaches that an addition of a signal sequence to pol-endo provides a useful system to investigate the hierarchy of signals involved in protein localization (page 352, col.2).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the SIV-pol gene product of Gŏttlinger by incorporating a secretory signal sequence at 5' end of the SIV-pol gene in view of Morris-Vasios. One would have been motivated to do so to produce a recombinant pol-gene product. One would have as reasonable expectation of success, since making recombinant proteins has been routine in the art. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gŏttlinger et al (US 6479281, 2002) in view of Morris-Vasios et al. (J Virol 62:349-353, 1988). as applied to claim 24 above, and further in view of Hazama et al. (Vaccine 11:629-36, 1993).

The instant claim is directed a plasmid carrying a SIV-derived pol gene encoding for a reverse transcriptase and an integrase, wherein the secretion protein is glycoprotein D of herpes simplex virus.

Gŏttlinger teaches a lentiviral vector system, wherein the vector system further comprising a pol vector encoding lentiviral pol-proteins operably linked to promoter and a polyadenylaltion sequence (col.27 lines 28-31). The cited art further teaches that the lentiviral pol protein that is selected form simian immunodeficiency virus (SIV).

Morris-Vasios teaches the fusion of the 5'-end the gene encoding avian sarcoma-leukosis retrovirus pol-endo protein to a secretory signal sequences obtained from interleukin-2 receptor gene (Abstract, page 351, left col. line 2-3, page 352, fig-5). The cited art further teaches the c-terminal portion of the pol gene product is required for the integration of proviral DNA into a

host cell chromosome (page 349, col.1). The cited art further teaches a recombinant p36 pol-endo protein containing a N-terminal secretory signal (page 352, fig-1). The cited art further teaches that addition of the secretory signal sequence directs the protein to secretory pathway (page 352, col.1). The cited art further teaches that an addition of a signal sequence to pol-endo provides a useful system to investigate the hierarchy of signals involved in protein localization (page 352, col.2). However, Gőttlinger and Morris-Vasios do not teach the fusion of SIV pol gene to a secretory sequence selected from a glycoprotein D of herpes simplex virus.

Hazama teaches that the fusion protein (t-gD-IL2) elicits superior protective immunity against HSV infection, involving high antibody response and HSV-specific cytotoxic lymphocytes. The cited art further teaches that these potentiated responses are due to a receptor-mediated targeting effect of IL-2 portion in immune cells (page 630, col.1, page 632, table-1).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the teaching of Gőttlinger and Morris-Vasios who suggest the incorporation of secretory signal sequence at 5' end of the SIV-pol gene with the secretory protein of glycoprotein D of herpes simplex virus. One would have been motivated to fuse the HSV gD to SIV pol gene products to make a recombinant protein that would have more immunogenic as compared to native protein. One would have been motivated to do so produce antibodies against SIV pol gene product as claimed. One would have a reasonable expectation of success, since making a recombinant protein and antibodies against the protein has been routine in the art. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-8724 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
Patent examiner

JAMES KETTER
PRIMARY EXAMINER